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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/389,565	09/03/1999	DAVID M. NEVILLE, JR.	14028.0290	5574

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EXAMINER

EWOLDT, GERALD R

ART UNIT

PAPER NUMBER

1644

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37

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/389,565

Applicant(s)

Neville et al.

Examiner

G.R. Ewoldt

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 7/01/02 and 2/14/03
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 30-33 and 37-42 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 30 and 38-42 is/are rejected.
- 7) ☒ Claim(s) 31-33 and 37 is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 28, 36
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. The IDS, filed 7/01/02, and the amendment, response, IDS, and declaration under 37 CFR 1.132 of Inventor Neville, filed 2/14/03, have been entered.
2. Claims 30-33 and 37-42 are pending and being acted upon.
3. In view of the remarks and declaration under 37 CFR 1.132 of Inventor Neville, filed 2/14/03, demonstrating the unexpected properties of the scFv UCHT1-DT390 construct, the obviousness rejection of Claims 31-33 and 37 under 35 U.S.C. 103(a) has been withdrawn.
4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).
5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.
6. Claims 30 and 38-42 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Chaudhary et al (V on form PTO-892) in view of Neville et al (AJ on form PTO-1449 filed December 6, 1999), Hirsch et al (AS on form PTO-1449 filed December 6, 1999) and Whitlow et al (74A on form PTO-1449 filed December 6, 1999),

all of record, for the reasons of record as set forth in Paper No. 27, mailed 6/13/02.

Applicant's arguments, filed 2/14/03, have been fully considered but they are not persuasive. Applicant argues that "features of the claimed constructs are surprising and unexpected over the prior art." Applicant indicates that "In the Declaration attached hereto as Appendix B, Dr. Neville provides additional data that proves the relative unpredictability of the properties of immunotoxin fusion proteins." Applicant concludes with "It was only by constructing the immunotoxin fusion protein and assessing its function that one skilled in the art can ascertain how effective a specific immunotoxin fusion protein was."

Given the submission of data in the declaration under 37 CFR 1.132 of Inventor Neville, the Examiner concedes that the scFv UCHT1-DT390 construct comprises unexpected and unpredictable properties. Accordingly, the rejection of Claims 31-33 and 37 has been withdrawn. However, given Applicant's concession that said properties are unexpected and unpredictable, as well as Applicant's statement that, "It was only through trial and error that the inventors, or others skilled in the art, could have determined that the claimed immunotoxin fusion protein was vastly superior," it is clear that the properties of the single tested construct cannot be extended to include the generic construct of Claim 30.

Inventor Neville makes some attempt in his 1.132 declaration to ascribe the unexpected properties of the scFv UCHT1-DT390 construct to the UCHT1 portion, however, the Inventor provides no factual demonstration of this assertion. It is just as likely that the unexpected properties are due to the DT390 portion of the construct. It is even more likely that the unexpected properties are due to an unexpected synergism between the two components of the construct. This appears to be the Inventor's actual position also, given his statement that "However, the state of the art at the time of the invention, and even now, was such that one skilled in the art could not predict the relative success of a binding pocket of a given scFv moiety when placed carboxy-terminal to DT390 in a fusion protein." Accordingly, Applicant's remarks and the Inventor's 1.132 declaration are insufficient to overcome the obviousness rejection of the generic invention as they provide no demonstration of any unexpected and unpredictable properties that can be extended to include the generic construct of Claim 30.

7. Claims 21-42 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Chaudhary et al (V on form PTO-892) in view of Neville et al (AJ on form PTO-1449 filed December 6, 1999), Hirsch et al (AS on form PTO-1449 filed December 6, 1999), Whitlow et al (74A on form PTO-1449 filed December 6, 1999) and Youle et al (V on form PTO-892), all of record, for the reasons of record as set forth in Paper No. 27, mailed 6/13/02.

Applicant's arguments, filed 2/14/03, have been fully considered but they are not persuasive. Applicant has not traversed this rejection separately. See the Examiner's arguments in section 6, above.

8. The following are new grounds for rejection.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 38-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention.

The method of the instant claims comprises treating essentially all diseases/conditions in which T cells are thought to play a part, ranging from transplant rejection, to malignancies (T cell leukemias), to a viral infection (AIDS), to all autoimmune diseases by administering a T cell toxin. Note that the value of eliminating the entire T cell population in a

subject as an effective treatment for many of the diseases encompassed by the claims must be questioned. For example, the elimination of all T cells as a treatment for AIDS would seem unacceptable given the fact that the prognosis of the disease is characterized by T cell counts, i.e., low counts indicate a worse prognosis. Also note that the claims encompass all autoimmune diseases, even though many, such as systemic lupus erythematosus and myasthenia gravis are known to be B cell, not T cell, mediated.

Given the incredible breadth of the claims, encompassing unrelated diseases of unrelated etiologies and pathologies, a significant enabling disclosure would be required. In particular, it is unlikely that any disclosure short of significant *in vivo* data would be able to overcome the unpredictability of methods encompassing effective treatments for such a diverse array of diseases/conditions. The specification, however, discloses no data significant to the claimed method in which the constructs of the instant claims are employed. Indeed, the bulk of the relevant Examples simply disclose how to make the scFv UCHT1-DT390 construct. Accordingly, the claimed method is considered to be highly unpredictable and requiring of undue experimentation to practice as claimed.

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of sufficient working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention.

11. No claim is allowed.

12. Claims 31-33 and 37 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claims.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are

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unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone numbers are 703-872-9306 (before final) and 703-872-9307 (after final).



G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600
April 22, 2003